TITLE: Age Dependent Alterations Induced by Transmeridian Flights in Airline Pilots

# AGE DEPENDENT ALTERATIONS INDUCED BY TRANSMERIDIAN FLIGHTS IN AIRLINE PILOTS

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**Running head:** Changes in transmeridian flights

**Abstract.**

Desynchronization among body rhythms and with the environment appears to be linked with *jet lag*, which may depend on many factors, including age, flight direction and number of time-zones crossed. To analyze this chronobiological state, we performed a multivariate analysis of the circadian system of airline pilots younger and older than 50 years, in Madrid-México-Madrid (-7 time zones, n=12) and Madrid-Tokyo-Madrid (+8 time zones, n=21) flights. Telemetrical devices were used to record pilots' locomotor activity, skin temperature and heart rate, during the flights to and from destiny, and one day after returning to Madrid.In addition the excretion of 6 sulphatoxy melatonin and free cortisol was measured in 6 hourly intervals during the whole period.. Time series were analised by cosinor and the rhythms were compared by ANOVA and Tukey contrasts. Age (under and over 50 years old) and flight direction groups were considered. Different psychometric tests were carried out at different times of the fligths in order to know how pilots are affected by transmeridian flights. Subjective time estimation was also recorded, as well as other psychological variables including anxiety, tiredness and performance. Activity / rest and heart rate rhythms are easily adapted to the new time zones whereas temperature rhythms manifest a rigid response after the phase shifts. Subjective time tended to be overestimated without exhibiting a clear circadian component. Psychometric evaluation showed that desinchronization affects all the pilots. Some results show an age-related variability with more marked influence in younger pilots, while no consistent effects of the flight direction were found.

*Keywords:* Jet lag; circadian rhythms; airline pilots; temperature; locomotor activity; heart rate, anxiety, tiredness, performance

## Introduction

Biological rhythms are the result of two interacting components: an endogenous one called biological clock and an exogenous, time-giver component or a *zeitgeber* (2,16) that is determined by the Geophysical variables. The synchrony between these components is the obvious adaptative value of the rhythms (13, 55, 60).
Circadian rhythms (i.e., with periods of about 24 h) disorders are focused especially on the alterations of entrainment pathways, that can be related to internal causes or with ageing and blindness (12). Exogenous alterations are caused by a mismatch between the body circadian rhythms and the environmental *zeitgebers* (13, 29, 31) as for example during Jet lag in which time-zone travellers encounter a pattern of light and darkness, activity, and social schedules shifted in time. The endogenous circadian system is slow to adapt to new time cues raising physiological and behavioral problems that are manifest until the correct phase relationship between biological rhythms and external *zeitgebers* is established. (15, 19).
After time-zone transitions, body rhythms become out of phase with the light/dark *zeitgeber*, and a new steady state is reached after reactive and predictive homeostatic mechanisms (3). Therefore they will be out of phase with each other during the process producing a temporal internal disorder or internal desynchronization, which is responsible for the general malaise, disturbed sleep, loss of mental efficiency, anxiety, irritability, tiredness and gastric disorders which are commonly reported in the first week or so after a long haul flight (20, 24, 31). These symptoms seem to increase with the number of time zones crossed (9,25) and age. There are not many studies concerning the population most at risk of being affected by transmeridian long-haul flights, i.e., the airline pilots although these alterations might have important effects in them. Here we present the results of a 2 yr. field study of Spanish pilots flying the routes from Madrid (Spain) to Mexico City (Mexico) or from Madrid to Tokyo (Japan). A number of physiological (locomotor activity, temperature, heart rate,hormonal excretion) and psychological (anxiety, tiredness, performance, etc.) variables were simultaneously recorded throughout the

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whole flight schedule taking into consideration the age of the individuals. Subjective time estimation recordings, were also performed as well as measurements of the urinary excretion of melatonin and free cortisol

**Methods.**

***Subjects***
Volunteers were male pilots of IBERIA airlines involved in transmeridian westward flights of the route Madrid-México-Madrid, (-7 time zones between Madrid and México, n=12). They were divided in two age groups: <50-yearold (n=5, average age 38.6±5.7 SD, range 31 to 47 yr), and >50- year old (n=7, average age 58.0 ± 1.0 SD, range 57 to 59 yr). The eastward flights were Madrid-Tokyo-Madrid, (+8 time zones, n= 21), and the groups of age were <50 years (n= 11, average age 38.7 ±2.1, range 35 to 42 yr), and> 50 (n= 10, average age 55.1 ± 2.2 SD, range 53 to 58 yr).

***Recordings***
Six days of continuous telemetrical recording were completed: the two days before the flight in Madrid were considered as baseline values (MAD1). The two days at the layover (MEX or TOK) were taken as "destiny" recordings, and the returning flight and the day after it in Madrid (MAD2) was used as the "post-flight" parameter. Recordings were performed with the Mini-Logger® series 2000 system (Minimitter Co., Inc., Sunriver, OR). Locomotor activity sensors were piezoelectric cristals of mercury located in a wristlet. Skin temperature recordings were performed to estimate core temperature because chronical rectal probes were inadequate in this experimental situation at the actual work site of the subjects. Callibrated sensors were located in chest belts to register heart rate.

**Psychological tests**

In order to evaluate pilots'anxiety and fatigue, we used: the S.T.A.I. (State-Trait Anxiety Inventory) of Spielberg (23) adapted to the Spanish population by Seisdedos Cubero (1994). The last part of this test (anxiety trait) was scored only once before the departure flight. A part of this instrument (question 8) was used as a reference of the changes in fatigue levels. In order to evaluate the alertness and perceptive state of the pilots, we used the Identical Figure test (Thurstone 1986) (27).. and the Perceptive-Spacial test (Seisdedos Cubero 1990) (22). All these measurements were carried out just at the beginning of the study in Madrid,_before and at the end of the flights (**forward and return**), during the stopover days, and finally 24h after returning to Madrid. Non flying persons remaining in Madrid (n=10) served as controls.

**Urine samples**

Urine samples were collected in 6 hour periods (00:00-06:00, 06:00:12:00, 12:00-18:00,and 18:0024:00 )over the six days of the study. The volume of each sample was measured and recorded andaliquots were kept on dry ice until analysis. The excretion of 6- sulfatoxymelatonin and cortisol in each sample was measured by RIA using commercial kits (6-sulfatoxymelatonin kit,Stockgrand,Surrey UK; cortisol kit Incstar Co ,Minnesota,USA) All samples were measured in the same RIA to avoid interassay variation.

***Analysis***
The sampling interval was of 5 minutes in every measured variable. The original cosinor time series was studied by serial cosinor analysis. Analysis of variance (ANOVA) with one fixed factor and Tukey's tests were used to compare the circadian parameters. Acrophase (defined as the time when the maxima of variables occurred) maps were constructed for locomotor activity and temperature, plotting the acrophase value of both rhythms for the five days versus Madrid clocktime.

***Time estimation***
Time estimation assessment was performed with special software. This program offers a set of different durations of auditive stimuli, which the subject has to estimate and/or reproduce .The computer analyzed and characterized the different ratios between real and estimated values.

***Psychological variables***

To evaluate the modification of the psychological tasks two non-parametric tests (Mann-Whitney for non related samples, and Wilcoxon for related samples) were used.

**Results.**

*Activity/rest rhythms.*
Locomotor activity showed a clear 24-hour rhythm at baseline It exhibited a rapid phase shift at destinations both after México and Tokyo flights by a 7 hour-delay and an 8 hour-advance respectively, following the phase shift of the light/dark *zeitgeber*. In all cases, a Madrid-like acrophase was reestablished after the return flights to Madrid. Disrupted activity/rest rhythms were observed during the stopover with activity events occuring during the night as well as a significant decrement of the amplitude in both age groups after flights to Tokyo .No significant differences were detected among age groups.

*Temperature rhythms.*
Skin temperature recordings show a clear circadian rhythmicity, despite the large interindividual variations.

Acrophases were not clearly affected by the initial flight to either Tokyo or Mexico remaining at times corresponding to normal conditions in Spain. Amplitude decremented significantly after the flights to México in the older group

*Heart rate rhythms.*
Circadian-like rhythms could be observed in the age recordings average fluctuating around the normal range of physiological values. Acrophases were clearly phase shifted only in younger pilots after the flights to Mexico and Tokyo,together with a decrease in amplitude that was also evidenced in the Tokyo flight. No significant changes occur in those over 50 years of age.

*Time estimation*
A significant overestimation of time was observed at destination in each cathegory, independently of flight direction. The S/R ratio was reverted after returning from México, not after Tokyo flights, with overestimation persisting for at least 2 more days.

**Urinary hormonal excretion**

Data about the urinary excretion of 6 sulphatoxy melatonin have been previously reported ( 27 bis).Pilots flying both to Mexico an Tokyo showed a pattern of free cortisol excretion that was similar to that found in the control group,although with strong interindividual variations. Pilots older than 50 years of age exhibited lower excretory values than the younger ones (p<o.o2)

**Psychological Variables**

Anxiety levels were low in absolute terms, in all the pilots. However, younger pilots showed relatively higher levels of anxiety with respect to basal levels in several of the periods monitored. Surprisingly, we found that older and younger pilots had increased significantly(p<o.o5) the anxiety levels during the second stopover day, especially the younger group (10% older - 40% younger). This profile was not found in eastward flights In contrast, the pilots under 50 mantained high levels of anxiety during the first stopover day and had a decrease during the second stopover day. Returning from Tokyo, the younger pilots had a anxiety peak at the end of the return flight and this score was the highest_studied (16.8 ± 7.8) and very significant ($p<0.01$) in comparison with the basal levels. Again, most of the pilots of this subgroup were young.

The pilots showed two peaks of tiredness at the end of every flight, both in west and in eastbound flights During westward flights pilots showed an earlier recovery than in eastward flights. A difference between old and young pilots existed in eastbound flights, the latter showing significantly higher levels of tiredness ($p< 0.05$).

Older pilots showed less improvement in the execution of attentional-perceptive_tasks than controls or younger pilots as demonstrated in the Identical Figure Test and in the Spacial Test

**Discussion**

Time zone transitions imposed by rapid long haul transmeridian flights present the possibility of studing the human circadian system. (4, 16). After phase shifts of the light/dark cycle induced by the flights, core temperature rhythm manifests a slow rate of entrainment, while heart rate and activity/rest rhythms are entrained faster due to their plastic phase responses.
Skin temperature variations may represent a good estimator of the core temperature rhythm (29) and can be measured as physiological correlates of performance, alertness/fatigue, and the sleep/wake rhythm (7). When temperature rises, alertness is maximal. In contrast , when the body temperature values begin to decrease, falling asleep is easier. Therefore, performance decrements during reentrainment of the body rhythms (7, 20, 31) are associated with a non-consolidate night sleep (25)
Heart rate rhythmicity exhibits a large interindividual variation (5,7,11).
Locomotor activity, might be influenced by the motivational state of the pilots and the social *zeitgeber* at the different destinations.
Skin temperature rhythms, show a rigid phase response to light/dark cycle phase shifts, probably related to core temperature (29). Disturbed nocturnal sleep during the stopover, was associated with a desynchronization between temperature and activity/rest rhythms.
With aging, adaptation to time zone transitions appears to be more difficult (10, 14, 17, 26). Tolerance to jet lag is evaluated by means of the magnitude of amplitude (10,14,17). In our study, we found that activity and heart rate rhythms of the under 50-yr old group remained coupled during reentrainment, which didn't occur in older age group. The abnormal position of temperature acrophases in the over 50-yr old group could be attributed to the weak expression of elderly temperature rhythms.
Although large shifts in urinary cortisol levels could be overseen by employing 6 h sampling intervals the data suggest that the pattern remains bound to Madrid time during all the period,thus being out of phase with the external environment.Harma et al ( 10 bis ) reported a 6 hour delay within 4 days after westward flights in a group of flight attendants .
Subjective time estimation did not exhibit circadian-like responses after the temporal alteration.. Therefore, the

relative failure in temporal estimation could be attributed to fatigue and stress caused by long haul flights.

It is generally accepted that delays of light/dark cycle (i.e., after westward journeys) produces less jet lag symptoms than advances (eastward journeys) (13, 4). In our case, we did not find any marked effect of flight direction on the circadian parameters being analysed. More precise measures of oscilator outputs (i.e., utilizing rectal probes for temperature) should be used in order to remove exogenous influences (13), a consideration that exceeds the objectives of the present study.

The findings in the present investigation suggest that an active reentrainment process start during the stopover, and may require several days in order to be completed. If a long rest strategy is choosen, aircrew would be exposed systematically to a reentrainment process, while a short stopover time, although less threatening to the body clock, probably would not allow pilots to have the necessary rest and alertness for the returning flight

Psychological alterations were always very moderate. Anxiety was low in all the pilots. This finding is not surprising, since pilots are trained to face emergency situations. Younger pilots exhibited the highest anxiety levels in both flight directions. In eastbound flights levels of anxiety are asociated with high levels of tiredness after the return flight. Also in eastbound flights, anxiety level was higher than in westbound flights and more pilots repeated high scores in different evaluations.

Anxiety levels increased in the second stopover day in westbound flights, especially in young pilots, coinciding with increased tiredness and decreased performance. Nicholson (18) found similar results in these directional trips. As expected, tiredness was maximum at the end of the trip to destination and return flights, but it was highest in the eastward flights and in pilots under_50, associated to the more marked levels of anxiety.

Performance increased in all the subjects due to the learning process linked to the repetitive execution of the same test. Non flying controls always obtained the highest scores in the Identical Figure test, followed very closely by younger pilots, whereas pilots over 50 yr. got the lowest suggesting that the biological circadian rythm of the older pilots remains in close synchronyzation with Madrid. This also justifies the poorer results obtained during the flights and the recovery after resting in Madrid.

Our results suggest that commercial pilots have adequate adaptation strategy to afront westbound flights of long duration. The return flight has the additional problem of a long night to which pilots have only parcially adaptated. In contrast, eastbound flights, cause a clear disruption of all studied variables.

Alternative strategies for improving jet-lag symptoms are currently under experimentation, including the pharmacological use of chronobiotics (agents which modify clock activity) (1, 9, 18) or the stimulation of the circadian system with bright lights at specific times of the cycle (6, 8, 21, 30).

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